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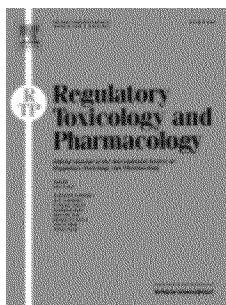
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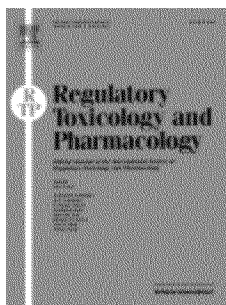
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Epidemiologic studies of glyphosate and cancer: A review

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Abstract

The United States Environmental Protection Agency and other regulatory agencies around the world have registered glyphosate as a broad-spectrum herbicide for use on multiple food and non-food use crops. Glyphosate is widely considered by regulatory authorities and scientific bodies to have no carcinogenic potential, based primarily on results of carcinogenicity studies of rats and mice. To examine potential cancer risks in humans, we reviewed the epidemiologic literature to evaluate whether exposure to glyphosate is associated causally with cancer risk in humans. We also reviewed relevant methodological and biomonitoring studies of glyphosate. Seven cohort studies and fourteen case-control studies examined the association between glyphosate and one

or more cancer outcomes. Our review found no consistent pattern of positive associations indicating a causal relationship between total cancer (in adults or children) or any site-specific cancer and exposure to glyphosate. Data from biomonitoring studies underscore the importance of exposure assessment in epidemiologic studies, and indicate that studies should incorporate not only duration and frequency of pesticide use, but also type of pesticide formulation. Because generic exposure assessments likely lead to exposure misclassification, it is recommended that exposure algorithms be validated with biomonitoring data.

Highlights

► We reviewed epidemiologic studies of glyphosate and cancer outcomes. ► We identified seven cohort studies and fourteen case-control studies. ► Our review found no consistent pattern of positive associations with any cancer. ► We recommend that exposure algorithms be validated with biomonitoring data.

Abbreviations

- AHS, Agricultural Health Study;
- CAS, Chemical Abstract Service;
- CI, confidence interval;
- FFES, Farm Family Exposure Study;
- HCL, hairy cell leukemia;
- IARC, International Agency for Research on Cancer;
- MGUS, monoclonal gammopathy of undetermined significance;
- NHL, non-Hodgkin lymphoma;
- OR, odds ratio;
- RR, relative risk;
- SLL/CLL, small lymphocytic lymphoma/chronic lymphocytic leukemia;
- US EPA, United States Environmental Protection Agency

Keywords

- Cancer;
- Glyphosate;
- Herbicides;
- Epidemiology

1. Introduction

Glyphosate(N-phosphonomethyl glycine; CAS registry #38641-94-0) is the primary active ingredient in Roundup-branded herbicides produced by the Monsanto Company. The United

States (US) Environmental Protection Agency (EPA) and other regulatory agencies around the world have registered this chemical as a broad-spectrum herbicide for use on multiple food and non-food use crops. Glyphosate-based herbicides, which have been sold in the US since 1974 and marketed under the brand names Roundup®, Roundup Pro®, Roundup PowerMAX™, Roundup WeatherMAX®, and AquaMaster®, are now registered in over 130 countries to control annual and perennial weeds, woody brush, and trees in agricultural, industrial, forestry, greenhouse, rights-of-way and residential areas. Other brands and manufacturers of glyphosate products include but are not limited to Glyphos® (Cheminova), Durango® DMA® (Dow AgroSciences), and Touchdown HiTech® (Syngenta). In the US, glyphosate (isopropylamine salt) herbicides were applied to 31% of all planted corn acres in 2005 ([USDA, 2006](#)) and 92% of all planted soybean acres in 2006 ([USDA, 2007](#)).

Glyphosate is widely considered by regulatory authorities and scientific bodies to have no carcinogenic potential ([EC, 2002](#), [US EPA, 1993](#) and [WHO/FAO, 2004](#)). US EPA has classified glyphosate as a Group E carcinogen, which is defined as having “evidence of non-carcinogenicity for humans” ([US EPA, 1993](#)). This classification was based on “a lack of convincing evidence of carcinogenicity in adequate studies with two animal species, rat and mouse” ([US EPA, 1993](#)). Negative results were observed in genotoxicity studies conducted under good laboratory practice conditions and compliant with current regulatory test guidelines ([Williams et al., 2000](#)). It was concluded that, in the absence of carcinogenic potential in animals and given the lack of genotoxicity in standard tests, glyphosate is unlikely to pose a carcinogenic risk to humans ([WHO/FAO, 2004](#) and [Williams et al., 2000](#)). In addition, US EPA has concluded that there is a reasonable certainty that no harm will result to the general population or to infants and children from aggregate exposure to residues of glyphosate ([US EPA, 2007](#)). Nevertheless, there has been no published comprehensive review of the epidemiologic research on this topic.

We reviewed epidemiologic cohort and case-control studies of glyphosate and cancer to evaluate whether exposure to glyphosate is associated causally with risk of developing cancer in humans. In addition, we reviewed methodological and biomonitoring studies of glyphosate to allow for a more comprehensive discussion of issues related to exposure assessment (including exposure misclassification and information bias) and other interpretation issues as they relate to findings from the epidemiologic studies. We did not consider it appropriate to calculate quantitative summary relative risk estimates across studies evaluating different site-specific cancers (e.g., breast cancer, brain cancer, esophageal cancer, etc.), and therefore did not conduct a meta-analysis.

2. Methods

Studies were included in our review if they met the following criteria: (1) published in a peer-reviewed journal; (2) English language; (3) analytic epidemiologic studies (e.g., cohort, case-control) that evaluated the association between glyphosate and a cancer outcome(s). Analyses of more general categories of “pesticides” or “herbicides” did not meet our criteria. Studies of poisonings or other acute effects of glyphosate were not included.

Multiple search strategies were employed to identify literature related to glyphosate exposure

and human cancer outcomes. A PubMed search was conducted using the term “glyphosate,” as well as its synonyms, chemical name, and Chemical Abstract Service (CAS) number, in conjunction with various terms related to epidemiology studies (e.g., “cohort,” “case-control”). In addition, broader searches for articles regarding epidemiologic studies of organophosphorus compounds used as pesticides or herbicides were conducted, as well as a search for case-control studies of pesticides or herbicides.

A separate search was conducted using the STN search service index, which searches multiple databases simultaneously, including Biosis, EMBASE, Medline, Pascal, and SciSearch. The CAS registry number for glyphosate was searched in combination with epidemiologic terms.

After duplicates were removed, abstracts were reviewed to determine if they met the inclusion criteria. Articles meeting the inclusion criteria were then obtained and reviewed.

Literature searches to identify biomonitoring studies of glyphosate were also performed using PubMed. We searched on the terms “glyphosate” and “Round up OR Roundup” in separate searches. Both searches also included the term “biomonitoring” as well as related terms including “sample,” “urine,” and “blood.” Abstracts identified from these searches were reviewed. For all articles of interest, the “related articles” identified by PubMed were also reviewed. All relevant articles were obtained.

For completeness, we examined the reference sections of the primary epidemiology and biomonitoring publications for additional articles that may not have been identified by the PubMed searches.

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